II. REMARKS

Claims 1 to 29 are pending in the subject application. Claims 23 and 28 are presently under examination and claims 1 to 22, 24 to 27 and 29, are withdrawn from examination as a result of a requirement for restriction.

The specification has been amended to correct a typographical error introduced in the Preliminary Amendment filed August 10, 2002. Claim 28 has been amended to depend from claim 23 rather than claim 22. This amendment also corrects a typographical error. Support for the amendment to claim 23 is found in the application papers on page 23, line 20 to page 24, line 16. An issue of new matter is not raised by these amendments and entry thereof is respectfully requested.

In view of the preceding amendments and remarks, reconsideration and withdrawal of the objections and rejections set forth in the November 20, 2002 Office Action is respectfully requested.

35 U.S.C. § 132

The Office objected to the Preliminary Amendment filed August 10, 2002 on the ground that the amendment to page 44 of the specification introduced new matter. Applicants have reviewed the first paragraph of page 44 and have noted that a typographical error was introduced into the paragraph in the Preliminary Amendment. In accordance with the Office's suggestion, the introduction of the terms "a b" between Ig-like and domains, has been removed. In view of this amendment, reconsideration and withdrawal of the objection to the specification is respectfully requested.

35 U.S.C. § 112, Second Paragraph

Claims 23 and 28 stand rejected under 35 U.S.C. § 112, first paragraph on the ground that the use of the term "suitable tissue" is indefinite. Applicants respectfully traverse.

A claim is read in light of the specification. As noted in *S3 Inc. v. nVidia Corp.*, 259 F.3d 1364, 59 U.S.P.Q.2d 1745 (Fed. Cir. 2001):

> "The purpose of claims is not to explain the technology or how it works, but to state the legal boundaries of the patent grant. A claim is not 'indefinite' simply because it is hard to understand when viewed without benefit of the specification."

Id. at 1369.

Applicants' specification, on page 42, lines 6 to 9 states that

> "In another aspect, the modulation of cell-cell or cell-matrix adhesion is an increase or to enhance cell-cell or cell-matrix adhesion mediated by polycystin in a suitable tissue. As used herein, a "suitable tissue" includes any tissue which polycystin, i.e., polycystin-1 or polycystin-2, is expressed as been described above."

Additional disclosure of "suitable tissue" includes, but is not limited to page 17, lines 18 to 24; page 24, lines 13 to 16 and page 47, lines 20 to 28. Thus one of skill in the art, upon reading Applicants' disclosure, would have no doubt as to the scope of the claims. For this reason, the rejection is in error and should therefore be romvoed.

35 U.S.C. § 112, First Paragraph

Claims 23 and 28 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to be supported by enabling disclosure for the full scope of the claims. The Office argued that besides the antibodies to polycystin and the homophilic Ig-like domains, the specification fails to provide any guidance as to how to make and use any agent.

First, Applicants maintain that the Office has failed to meet its initial burden of providing a prima facie case to support the rejection. By law a patent application is presumptively enabled when filed. *In re Marzocchi*, 439 F.2d at 223, 169 U.S.P.Q. at 369. Moreover,

> . . . it is incumbent upon the Patent Office, whenever a rejection on [grounds of enablement] is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested

statement. Otherwise there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

Id. at 224, 169 U.S.P.Q. at 369-70. Indeed, as pointed out by the USPTO in the *Section 112 Enablement Training Manual* (citing *In re Wright*, 999 F.2d at 1561-62, 27 U.S.P.Q.2d at 1513), "the case law makes clear that properly reasoned and supported statements explaining any failure to comply with section 112 are a requirement to support a rejection."[1] The new *35 U.S.C. § 112 First Paragraph Enablement Training Manual*,[2] released by the USPTO in January, 2001, reinforces this requirement:

> When rejecting a claim under the enablement requirement of section 112, the examiner bears the "initial burden of setting forth a reasonable explanation as to why [he/she] believes that the scope of protection provided by [the] claim is not adequately enabled by the description of the invention provided in the specification." *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). To object to a specification on the grounds that the disclosure is not enabling with respect to the scope of a claim sought to be patented, the examiner must provide evidence or technical reasoning substantiating those doubts. *Id.*; and MPEP Section 2164.04.
>
> Without a reason to doubt the truth of the statements made in the patent application, the application must be considered enabling. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Marzocchi*, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971). The burden placed on the examiner is reflected in the MPEP Section 706.03.
>
> Accordingly, the case law makes clear that properly reasoned and supported statements explaining any failure to comply with Section 112 are a requirement to support a rejection. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).
>
> *Section II B of 35 U.S.C. § 112 First Paragraph Enablement Training Manua.*

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1 The USPTO Training Manual is available on-line at http://www.usUSPTO.gov by clicking on the following: "Site Index," "Office of Patent Policy Dissemination," "Special Training." See also, 66 Fed. Reg. 1099 (January 5, 2001).

2 Id.

The Office has failed to provide any technical or scientific reasoning why Applicants' disclosure fails to enable claims 23 and 28. Applicants disclose and enable more than antibodies to polycystin. See for example, page 47, lines 10 to 16:

> "Alternatively, this invention also provides methods to promote cell-cell or cell-matrix adhesion in a tissue by delivering to the cell or tissue an effective amount of polycystin-1 to the cell or a polypeptide comprising an Ig-like domain of polycystin to the cell or tissue. The polycystin is delivered in the form of a polynucleotide or polypeptide or protein. In addition, one can restore normal cell-cell or cell-matrix adhesion is a tissue containing soluble, mutated polycystin by removing or binding the mutated polycystin using the anti-polycystin antibodies described herein as well as those known in the art."

In the specification, Applicants note on page 30, lines 16 to 20 that:

> "In a further embodiment, an isolated polynucleotide encodes a polypeptide corresponding to the Ig-like domains in polycystin-1. Such polypeptides include, but are not limited to polypeptides comprising amino acids 843 to 1200 or 1205 to 1625 or 1626 to 2136, as shown in Figure 1."

The Office also asserted that claim 28 was enabled only as it applies to *in vitro* application of the method on the ground the specification provided one example of disruption of cell-cell adhesion *in vitro*. However, the Office has failed to provide any evidence why evidence of enhancement of cell-cell adhesion using the disclosed method to ***modulate*** cell adhesion would not be predictive of *in vivo* efficacy. Absent evidence to the contrary, Applicants assertion of enablement and utility are sufficient to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph.

For these reasons, the rejections under 35 U.S.C. § 112, first paragraph are improper and should be removed.

Patent Drawings Objections

New Figures are submitted herewith in response to the Notice of Patent Drawings Objections issued in connection with the first substantive Office Action. No new matter has been added. Consideration and entry of the substitute Figures are respectfully requested.

III. CONCLUSION

No fee is deemed necessary in connection with the filing of this response. However, if any fee is determined to be required, the Commissioner is hereby authorized to charge any additional fees which may be required by this paper, or credit any overpayment to Deposit Account No. 50-2518, Billing Ref. No. 219442-7214.

If a telephone interview would advance prosecution of the subject application, the Examiner is invited to telephone the undersigned at 650-849-4950.

Date: March 25, 2003

Respectfully submitted,

By: Antoinette F. Konski

Antoinette F. Konski
Registration No. 34,202

Bingham McCutchen LLP
Formerly McCutchen, Doyle, Brown & Enersen, LLP
Three Embarcadero Center
San Francisco, California 94111
Telephone: (650) 849-4950
Telefax: (650) 849-4800

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Paragraph beginning at line 1 of page 44 has been amended as follows:

Using antibodies against three different regions of polycystin- 1: N-terminal (LRR), C-terminal, and the middle region (REJ), the experiments described herein clearly showed that polycystin-1 was predominantly expressed at sites of cell-cell contact in kidney epithelial cells, as was the case for endothelial cells. The homophilic binding potential of several Ig-like [a b] domains, i.e., Ig^a , Ig^b and Ic^e, containing 4, 5 and 6 domains, as clusters were analyzed as described below. Each region was translated *in vitro* and tested for the ability to bind to each region including itself in the form of immobilized fusion protein. The binding properties of all combinations were quantitatively analyzed as a percentage of binding of *in vitro* translated protein. In this type of assay the fusion proteins are present in a vast excess compared to the amount of the translated probe. Therefore, theoretically almost all of the translated probe should bind to immobilized fusion protein, even if binding is weak. Phizicky, F.M. & Fields, S. (1995) Microbiological Reviews **59**:94-123. In practice, deviations from quantitative binding occur if not all of the immobilized protein or/and *in vitro* translated probe is functionally active. Nevertheless, a functionally relevant interaction should result in significant retention of ligand. For example, estimates from affinity chromatography binding experiments on the N-NusA, NusA-RNA polymerase and RAP3O/74-RNA polymerase II interactions indicate that at least 50% of these proteins are available for binding. Formosa, I. et al. (1991) Meth. Enzymol. **208**:24-45.

In the claims:

Claim 28 has been amended as follows:

28. (Amended) The method of claim [22] 23, wherein the modulation of cell-cell or cell-matrix adhesion is promotion or enhancement of cell-cell or cell-matrix adhesion in a suitable cell or tissue.

Pending Claims

23. A method for modulating cell-cell adhesion in a suitable tissue, comprising delivering to the tissue an effective amount of an agent that modulates the binding of polycystin in the tissue.

28. (Amended) The method of claim 23, wherein the modulation of cell-cell or cell-matrix adhesion is promotion or enhancement of cell-cell or cell-matrix adhesion in a suitable cell or tissue.